A TB Model With Infection-Age-Dependent Infectivity

Carlos Castillo-Chavez and Wenxiong Xu*

Biometrics Unit and Center For Applied Mathematics
Cornell University
337 Warren Hall,Ithaca,NY14853-7801,U.S.A.

April 6,1996

* Visiting Scholar from Xi'an Jiaotong University ,China

1.The basic model and its variant equivalent forms

It has been considered by Carlos Castillo-Chavez and Zhilan Feng(see[1]) that the following preliminary model for the transmission of tuberculosis(TB):

$$
\begin{aligned}
\frac{d}{dt}S &= \Lambda - \beta c S\frac{I}{N} - \mu S \\
\frac{d}{dt}L &= \beta c S\frac{I}{N} - (\mu + k + r_1)L + \beta' c\, T\frac{I}{N} \\
\frac{d}{dt}I &= kL - (\mu + d)I - r_2 I \\
\frac{d}{dt}T &= r_1 L + r_2 I - \beta' c\, T\frac{I}{N} - \mu T \\
N &= S + L + I + T
\end{aligned}
\tag{1}
$$

Where the host population is divided into the following epidemiological classes or subgroups:Susceptibles (S),Latent (L, infected but not infectious),Infectious (I) and (effectively) Treated (T) individuals. N denotes the total population.The parameter Λ is the recruitment rate,β and $\beta'$are respectively the average proportions of susceptible and treated individuals infected by one infectious individual per contact per unit of time, c is the per-capita contact rate, μ is the per-capita natural death rate, k is the rate at which an individual leaves the latent class by becoming infectious, d is per-capita disease induced death rate,and r_1 and r_2 are per-capita treatment rates.

It is worthwhile to pay attention that the parameters in model (1) shown above are all constant. Particularly , that k is equal to constant means that the rate at which an individual leaves the latent class by becoming infectious does not depend on the latent-age.This is not reasonable. In fact,the parameter k depends on the latent-age τ according to the real case (see [2]), i.e. $k = k(\tau)$ is the function of variable τ . So we should improve the model (1) and further consider the following basic model:

$$
\begin{aligned}
\frac{d}{dt}S &= \Lambda - \beta c S\frac{I}{N} - \mu S \\
\frac{d}{dt}L &= \beta c S\frac{I}{N} - (\mu + r_1)L - \int_0^\infty k(\tau)l(t,\tau)d\tau + \beta' c T\frac{I}{N} \\
\frac{d}{dt}I &= \int_0^\infty k(\tau)l(t,\tau)d\tau - (\mu + d)I - r_2 I \\
\frac{d}{dt}T &= r_1 L + r_2 I - \beta' c\, T\frac{I}{N} - \mu T \\
L &= \int_0^\infty l(t,\tau)d\tau \\
N &= S + L + I + T
\end{aligned}
\tag{2}
$$

Here,the parameter $\Lambda, \beta, \beta', c, \mu, d, r_1, r_2$ are all positive constants with the same epidemiological meanings as above. The function $k(\tau)$ with positive value is the infectious rate,

$l(t,\tau)$ is the density of infected but not infectious individuals. Clearly, the model (2) is equivalent to the following model in mathematical viewpiont:

$$
\begin{aligned}
\frac{d}{dt}S(t) &= \Lambda - B_1(t) - \mu S(t) \\
(\frac{\partial}{\partial t} + \frac{\partial}{\partial \tau})l(t,\tau) &= -(\mu + k(\tau) + r_1)l(t,\tau) \\
\frac{d}{dt}I(t) &= W(t) - (\mu + d + r_2)I(t) \\
\frac{d}{dt}T(t) &= r_1 L(t) + r_2 I(t) - B_2(t) - \mu T(t) \\
l(t,0) &= B_1(t) + B_2(t) \\
B_1(t) &= \beta\ c\ S(t)\frac{I(t)}{N(t)} \\
B_2(t) &= \beta' c\ T(t)\frac{I(t)}{N(t)} \\
W(t) &= \int_0^\infty k(\tau)l(t,\tau)d\tau \\
L(t) &= \int_0^\infty l(t,\tau)d\tau \\
N(t) &= S(t) + L(t) + I(t) + T(t)
\end{aligned}
\tag{3}
$$

By integrating along characteristic lines, we can reduce (3) to the following system of integral equations:

$$S = N^0 - B_1 * P_\mu + f_1 \tag{4a}$$

$$L = B_1 * P_{\mu+k(s)+r_1} + B_2 * P_{\mu+k(s)+r_1} + f_2 \tag{4b}$$

$$I = W * P_{\mu+d+r_2} + f_3 \tag{4c}$$

$$T = r_1 L * P_\mu + r_2 I * P_\mu - B_2 * P_\mu + f_4 \tag{4d}$$

$$W = B_1 * Q + B_2 * Q + f_5 \tag{4e}$$

$$B_1 = \beta\ c\ S\frac{I}{N} \tag{4f}$$

$$B_2 = \beta' c\ T\frac{I}{N} \tag{4g}$$

$$N = S + L + I + T \tag{4h}$$

Here ,we have use the notation

$$(B * P)(t) = \int_0^t B(t-\tau)P(\tau)d\tau$$

and

$$
\begin{aligned}
P_\alpha &= exp(-\int_0^\tau \alpha\ ds) \\
Q &= k(\tau)P_{\mu+k(s)+r_1}(\tau) \\
N^0 &= \frac{\Lambda}{\mu} \\
f_1 &= (S(0)-\frac{\Lambda}{\mu})\ e^{-\mu t} \\
f_2 &= \int_t^\infty l(0,\tau-t)\frac{P_{\mu+k(s)+r_1}(\tau)}{P_{\mu+k(s)+r_1}(t-\tau)}d\tau \\
f_3 &= I(0)\ e^{-(\mu+d+r_2)t} \\
f_4 &= T(0)\ e^{-\mu t} \\
f_5 &= \int_t^\infty l(0,\tau-t)k(\tau)\frac{P_{\mu+k(s)+r_1}(\tau)}{P_{\mu+k(S)+r_1}(\tau-t)}d\tau
\end{aligned}
\tag{5}
$$

In the following, we will respectively use the models (2),(3) and (4) for special purpose in different cases.

2.The existence of the stationary states and the basic reproductive number R_0

In this section ,we concentrate on the sdudy of the existence of the stationary states, that is, equilibria or time-indepentent solutions,that are candidates for the asymptotic behavior of the disease dynamics.

Using the Laplace transform notation, we can note

$$
\begin{aligned}
\hat{P}(0) &= \int_0^\infty P_{\mu+k(s)+r_1}(\tau)d\tau = \int_0^\infty exp(-\int_0^\tau (\mu+k(s)+r_1)ds)d\tau \\
\hat{Q}(0) &= \int_0^\infty Q(\tau)d\tau = \int_0^\infty k(\tau)exp(-\int_0^\tau (\mu+k(s)+r_1)ds)d\tau
\end{aligned}
$$

Then it can easily be checked that the equilibria of system (3) depend on the following equations:

$$
\begin{aligned}
&\Lambda-\beta cS\frac{I}{N}-\mu S=0 \\
&L-(\beta cS\frac{I}{N}+\beta' cT\frac{I}{N})\hat{P}(0)=0 \\
&(\beta cS\frac{I}{N}+\beta' cT\frac{I}{N})\hat{Q}(0)-(\mu+d+r_2)I=0 \\
&r_1L+r_2I-\beta' cT\frac{I}{N}-\mu T=0 \\
&S+L+I+T=N
\end{aligned}
\tag{6}
$$

We take a assumptation similar to [1] that the infection probabilities per contact for the treated class is the same as that of the susceptible class,i.e.,$\beta=\beta'$,and pay attention to the idential equation

$$r_1\hat{P}(0) + \mu\hat{P}(0) + \hat{Q}(0) = 1, \tag{7}$$

then the equations (6) turn to the following equivalent equations:

$$\begin{aligned}
&\Lambda - \mu N - dI = 0 \\
&L - \beta c(N - L - I)\frac{I}{N}\hat{P}(0) = 0 \\
&\beta c(N - L - I)\frac{I}{N}\hat{Q}(0) - (\mu + d + r_2)I = 0 \\
&\Lambda - \beta c S\frac{I}{N} - \mu S = 0 \\
&r_1 L + r_2 I - \beta c T\frac{I}{N} - \mu T = 0
\end{aligned} \tag{8}$$

For solving these equations above,let

$$q = \beta c(N - L - I)\frac{I}{N} \tag{9}$$

then,clearly

$$I = \frac{\hat{Q}(0)}{\mu + d + r_2}q \tag{10}$$

$$L = \hat{P}(0)q \tag{11}$$

$$N = \frac{\Lambda}{\mu} - \frac{d}{\mu}\frac{\hat{Q}(0)}{\mu + d + r_2}q \tag{12}$$

$$S = \frac{\Lambda}{\mu + \beta c\frac{I}{N}} \tag{13}$$

$$T = \frac{r_1 L + r_2 I}{\mu + \beta c\frac{I}{N}} \tag{14}$$

substitute (10),(11),(12) into (9),the parameter q satisfy the equation

$$q(\frac{\Lambda}{\mu} - \frac{d}{\mu}\frac{\hat{Q}(0)}{\mu + d + r_2}q) = \frac{\beta c\hat{Q}(0)}{\mu + d + r_2}q(\frac{\Lambda}{\mu} - \frac{d}{\mu}\frac{\hat{Q}(0)}{\mu + d + r_2}q - \hat{P}(0)q - \frac{\hat{Q}(0)}{\mu + d + r_2}q) \tag{15}$$

By analysing (15),we get the basic reproductive number

$$R_0 = \frac{\beta c\hat{Q}(0)}{\mu + d + r_2} \tag{16}$$

and the following threshold result for existence of an endemic equilibrium.

THEOREM 1.If $R_0 \leq 1$, there exists only the disease-free equilibrium $E^0(S^0, L^0, I^0, T^0)$, no other equilibria. If $R_0 > 1$,there is a unique endemic equilibrium $E^*(S^*, L^*, I^*, T^*)$ except the disease-free equilibrium E^0. Here

$$L^0 = I^0 = T^0 = 0, S^0 = N^0 = \frac{\Lambda}{\mu} \tag{17}$$

$$L^* = \hat{P}(0)q \tag{18}$$

$$I^* = \frac{\hat{Q}(0)}{\mu + d + r_2} q \tag{19}$$

$$T^* = \frac{r_1 L^* + r_2 I^*}{\mu + \beta c \frac{I^*}{N^*}} \tag{20}$$

$$S^* = \frac{\Lambda}{\mu + \beta c \frac{I^*}{N^*}} \tag{21}$$

and

$$N^* = \frac{R_0}{R_0 - 1}(L^* + I^*) \tag{22}$$

$$q = \frac{(R_0 - 1)\Lambda(\mu + d + r_2)}{d(R_0 - 1)\hat{Q}(0) + \mu R_0 \hat{P}(0)(\mu + d + r_2) + \mu R_0 \hat{Q}(0)} \tag{23}$$

Proof.

Solving (15) for q, cause two cases.

Case A. $q = 0$ as a solution of the equation (15), one finds $E^0(S^0, L^0, I^0, T^0)$ satisfied (17) from (10) – (14).

Case B. $q \neq 0$, then the equation (15) for q is equivalent to the following equation

$$(R_0 - 1)(\frac{\Lambda}{\mu} - \frac{d}{\mu}\frac{\hat{Q}(0)}{\mu + d + r_2} q) - R_0 \hat{P}(0) q - \frac{R_0 \hat{Q}(0)}{\mu + d + r_2} q = 0 \tag{24}$$

If $R_0 = 1$, no nonzero q satisfy (24).Thus there are no endemic equilibria from (10) – (14).

If $R_0 < 1$, no q satisfy (24) such that I, L, N expressed by (10),(11),(12) all are nonnegative and at least one of them is positive.So, there are no endemic equilibria.

If $R_0 > 1$,we can solve (24), get positive solution q expressed by (23) and find further (18) – (22) from(10) – (14).Particularly,one can check by (12) that

$$\begin{aligned}
N^* &= \frac{\Lambda}{\mu} - \frac{d}{\mu}\frac{\hat{Q}(0)}{\mu + d + r_2}\frac{(R_0 - 1)\Lambda(\mu + d + r_2)}{d(R_0 - 1)\hat{Q}(0) + \mu R_0 \hat{P}(0)(\mu + d + r_2) + \mu R_0 \hat{Q}(0)} \\
&= \frac{\Lambda R_0[(\mu + d + r_2)\hat{P}(0) + \hat{Q}(0)]}{d(R_0 - 1)\hat{Q}(0) + \mu R_0 \hat{P}(0)(\mu + d + r_2) + \mu R_0 \hat{Q}(0)} \\
&= \frac{R_0}{R_0 - 1}(L^* + I^*),
\end{aligned}$$

(22) holds and S^*, L^*, I^*, T^*, N^* all are positive. Thus the proof end.

3.Stability of the disease-free equilibrium E^0 and endemic equilibrium E^*

In this section,Fator's lemma and the following notation will be useful.For a bounded real-valued function f defined on $[0, \infty)$,we set

$$\begin{aligned} f_\infty &= \liminf_{t\to\infty} f(t), \\ f^\infty &= \limsup_{t\to\infty} f(t), \\ f(\infty) &= \lim_{t\to\infty} f(t). \end{aligned}$$

The following theorem connects the basic reproductive number R_0 to the extinction of the disease.

THEOREM 2. Let $R_0 < 1$. Then the disease-free equilibrium E^0 is globally attractive, i.e.,E^0 is globally asymptotically stable.

Proof.

We use the model formulation (4) and (5). First, we easily observe that

$$f_j(\infty) = 0, \qquad j = 1, ..., 5. \tag{25}$$

Then we can apply Fatou's lemma and Lebesgue's theorem of dominated convergence to (4) to get useful estimations in inequalitys and further complete our proof.

Let

$$B = B_1 + B_2, \tag{26}$$

from (4e),(4f),(4g),(4h) and the assumed condition $\beta' = \beta$, we get equation and inequality below

$$W = B * Q + f_5, \tag{27}$$

$$B = \beta c I \frac{S+T}{N} \leq \beta c I. \tag{28}$$

Further,by (25),(27),(28) and (4c), we get

$$W^\infty \leq B^\infty \hat{Q}(0) \tag{29}$$

$$B^\infty \leq \beta c I^\infty \tag{30}$$

$$I^\infty \leq W^\infty \int_0^\infty P_{\mu+d+r_2}(\tau) d\tau = \frac{1}{\mu+d+r_2} W^\infty \tag{31}$$

Introducing (30),(31) into (29),we get

$$W^\infty \leq R_0 W^\infty, \tag{32}$$

i.e.,

$$(1 - R^0)W^\infty \leq 0, \tag{33}$$

or,

$$W^\infty \leq 0. \tag{34}$$

Pay attention to $0 \leq W$ and (33), we find

$$W^\infty = W(\infty) = 0. \tag{35}$$

So, by (35),(31),(30) and $0 \leq I, 0 \leq B$, we find

$$I^\infty = I(\infty) = 0, \tag{36}$$

$$B^\infty = B(\infty) = 0. \tag{37}$$

Similarly, we can find

$$B_1(\infty) = B_2(\infty) = 0, \tag{38}$$

and

$$L(\infty) = T(\infty) = 0, \tag{39}$$

$$S(\infty) = N(\infty) = N^0 = \frac{\Lambda}{\mu}. \tag{40}$$

Synthesize (36),(39),(40),we find

$$(S, L, I, T) \to (\frac{\Lambda}{\mu}, 0, 0, 0) = E^0, \quad t \to \infty. \tag{41}$$

The proof end.

The following theorem show that the disease may be persistent.

THEOREM 3.The endemic equilibrium E^* is locally asymptotically stable if

$$\varepsilon = R_0 - 1 \tag{42}$$

is sufficiently close to 0 or $k(\tau) \equiv k$ (constant).

Proof.

From (2),we get

$$\frac{d}{dt}N = \Lambda - \mu N - dI. \tag{43}$$

So,in order to study the stability of E^* ,we only need considering following equivalent subsystem

$$\begin{aligned}
\frac{d}{dt}N &= \Lambda - \mu N - dI \\
(\frac{\partial}{\partial t} + \frac{\partial}{\partial \tau})l(t,\tau) &= -(\mu + k(\tau) + r_1)l(t,\tau) \\
\frac{d}{dt}I &= W(t) - (\mu + d + r_2)I \\
l(t,0) &= \beta c(N - I - L)\frac{I}{N} \\
W(t) &= \int_0^\infty k(\tau)l(t,\tau)d\tau \\
L(t) &= \int_0^\infty l(t,\tau)d\tau.
\end{aligned} \tag{44}$$

Set

$$\begin{aligned}
&N = N^* + n, \\
&l = l^* + u, \quad i.e., \quad L = L^* + v, \\
&I = I^* + i,
\end{aligned}$$

we linearize (44) around the endemic equilibrium E^* as follows

$$\begin{aligned}
\frac{d}{dt}n &= -\mu n - di \\
(\frac{\partial}{\partial t} + \frac{\partial}{\partial \tau})u(t,\tau) &= -(\mu + k(\tau) + r_1)u(t,\tau) \\
\frac{d}{dt}i &= \omega - hi \\
u(t,0) &= \frac{\beta c I^*}{N^*}(n - i - v) + \frac{\beta c}{N^*}(N^* - I^* - L^*)i \\
&\quad - \frac{\beta c}{N^*}\frac{I^*}{N^*}(N^* - I^* - L^*)n \\
\omega &= \int_0^\infty k(\tau)u(t,\tau)d\tau \\
v &= \int_0^\infty u(t,\tau)d\tau
\end{aligned} \tag{45}$$

here,

$$h = \mu + d + r_2.$$

To study the stability of this linear system (45) we look of solutions to (45) of the exponontial form

$$\begin{aligned}
n(t) &= e^{zt}\tilde{n}, \\
u(t,\tau) &= e^{zt}\tilde{u}(\tau), \\
i(t) &= e^{zt}\tilde{i}
\end{aligned} \tag{46}$$

with a complex number z and $\tilde{n} \neq 0, \tilde{u}(\tau) \not\equiv 0, \tilde{i} \neq 0$.

The endemic equilibrium will be locally asymptotically stable, provided that, for all solutions of this form (46), the real part of z is strictly negative. It will be unstable if there is at least one such solution with the real part of z being strictly positive.

Substituting (46) into (45) yeilds

$$z\tilde{n} = -\mu\tilde{n} - d\tilde{i} \tag{47a}$$

$$z\tilde{u}(\tau) + \frac{d}{d\tau}\tilde{u}(\tau) = -(\mu + k(\tau) + r_1)\tilde{u}(\tau) \tag{47b}$$

$$z\tilde{i} = \tilde{\omega} - h\tilde{i} \tag{47c}$$

$$\begin{aligned}\tilde{u}(0) &= \beta c(\tilde{n} - \tilde{v} - \tilde{i})\frac{I^*}{N^*} - \frac{\tilde{n}}{N^*}\beta c(N^* - L^* - I^*)\frac{I^*}{N^*} \\ &\quad + \frac{\tilde{i}}{N^*}\beta c(N^* - L^* - I^*)\end{aligned} \tag{47d}$$

$$\tilde{v} = \int_0^\infty \tilde{u}(\tau)d\tau \tag{47e}$$

$$\tilde{\omega} = \int^i nfty_0 k(\tau)\tilde{u}(\tau)d\tau \tag{47f}$$

Using the Laplace transform notation again, we note

$$\begin{aligned}\hat{P}(z) &= \int_0^\infty e^{-z\tau}P_{\mu+k(s)r_1}(\tau)d\tau \\ &= \int_0^\infty exp(-\int_0^\tau (\mu + k(s) + r_1 + z)ds)d\tau,\end{aligned} \tag{48}$$

$$\begin{aligned}\hat{Q}(z) &= \int_0^\infty e^{-z\tau}Q(\tau)d\tau \\ &= \int_0^\infty k(\tau)exp(-\int_0^\tau (\mu + k(s) + r_1 + z)ds)d\tau.\end{aligned} \tag{49}$$

Solve (47b) for $\tilde{u}$ and fit the result into (47e) and (47f) as follows

$$\tilde{v} = \tilde{u}(0)\tilde{P}(z), \tag{50}$$

$$\tilde{\omega} = \tilde{u}(0)\tilde{Q}(z). \tag{51}$$

By (47c) and (51), we find

$$\tilde{i} = \frac{1}{h+z}\tilde{u}(0)\tilde{Q}(z), \tag{52}$$

By (47a) and (52), we find

$$\tilde{n} = \frac{-d}{\mu + z}\frac{1}{h+z}\tilde{u}(0)\tilde{Q}(z). \tag{53}$$

Note that $\tilde{u}(0)$ must be different from zero because otherwise both $\tilde{n} = 0, \tilde{i} = 0$ at least.Fitting (50),(52),(53) into (47d) and dividing by $\tilde{u}(0) \neq 0$ yeilds the characteristic equation

$$\begin{aligned}
1 =& \beta c(\frac{-d}{\mu+z}\frac{1}{h+z}\hat{Q}(z) - \hat{P}(z) - \frac{1}{h+z}\hat{Q}(z))\frac{I^*}{N^*} \\
&+ \frac{1}{N^*}\frac{d}{\mu+z}\frac{1}{h+z}\hat{Q}(z)\beta c(N^* - L^* - I^*)\frac{I^*}{N^*} \\
&+ \frac{1}{N^*}\frac{1}{h+z}\hat{Q}(z)\beta c(N^* - L^* - I^*)
\end{aligned} \tag{54}$$

Substituting $(18)-(23)$ and (42) into (54),we get

$$\begin{aligned}
1 =& \frac{\varepsilon h}{h\hat{P}(0) + \hat{Q}(0)}(\frac{-d}{\mu+z}\frac{1}{h+z}\hat{Q}(z) - \frac{1}{h+z}\hat{Q}(z) - \hat{P}(z)) \\
&+ \frac{\varepsilon h\hat{Q}(0)}{(1+\varepsilon)(h\hat{P}(0) + \hat{Q}(0))}\frac{d}{\mu+z}\frac{1}{h+z}\frac{\hat{Q}(z)}{\hat{Q}(0)} + \frac{h}{h+z}\frac{\hat{Q}(z)}{\hat{Q}(0)}
\end{aligned} \tag{55}$$

To simplify the characteristic equation further, we define the probability densities

$$p(\tau) = \frac{P_{\nu+k(s)+r_1}(\tau)}{\hat{P}(0)}, \tag{56}$$

$$q(\tau) = \frac{Q(\tau)}{\hat{Q}(0)}, \tag{57}$$

and introduce the parameters

$$\delta_1 = \frac{h\hat{P}(0)}{h\hat{P}(0) + \hat{Q}(0)}, \tag{58}$$

$$\delta_2 = \frac{\hat{Q}(0)}{h\hat{P}(0) + \hat{Q}(0)}, \tag{59}$$

Then it is clear that

$$\hat{p}(z) = \int_0^\infty e^{-z\tau} p(\tau) d\tau = \frac{\hat{P}(z)}{\hat{P}(0)}, \tag{60}$$

$$\hat{q}(z) = \int_0^\infty e^{-z\tau} q(\tau) d\tau = \frac{\hat{Q}(z)}{\hat{Q}(0)}, \tag{61}$$

$$\int_0^\infty p(\tau) d\tau = \int_0^\infty q(\tau) d\tau = 1, \tag{62}$$

$$0 < \delta_1 < 1, \quad 0 < \delta_2 < 1, \quad \delta_1 + \delta_2 = 1. \tag{63}$$

We also express the complex numbers in (55) as forms

$$\frac{h}{h+z} = a e^{-i\ \theta_h}, \tag{64}$$

$$\frac{1}{\mu+z} = b e^{-i\ \theta_\mu}, \tag{65}$$

here,

$$a = \frac{h}{\sqrt{(h+x)^2+y^2}}, \tag{66}$$

$$b = \frac{1}{\sqrt{(\mu+x)^2+y^2}}, \tag{67}$$

$$cos\theta_h = \frac{h+x}{\sqrt{(h+x)^2+y^2}}, \tag{68}$$

$$sin\theta_h = \frac{y}{\sqrt{(h+x)^2+y^2}}, \tag{69}$$

$$cos\theta_\mu = \frac{\mu+x}{\sqrt{(\mu+x)^2+y^2}}, \tag{70}$$

$$sin\theta_\mu = \frac{y}{\sqrt{(\mu+x)^2+y^2}}, \tag{71}$$

and

$$z \equiv x + i\ y. \tag{72}$$

Clearly, the real numbers a, b satisfy

$$0 < a \leq 1, \quad 0 < b \leq \frac{1}{\mu}, \quad \forall z = (x,y) \in R_+^2 = \{(x,y) \mid x \geq 0, y \geq 0\}. \tag{73}$$

With these definitions and expressions above, (55) takes the form

$$1 = (1 - \varepsilon\ \delta_2 - \frac{\varepsilon^2}{1+\varepsilon}\delta_2\ b\ d\ e^{-i\ \theta_\mu})\ a\ e^{-i\ \theta_h}\hat{q}(z) - \varepsilon\ \delta_1 \hat{p}(z). \tag{74}$$

To sdudy the position of the roots $z = x + i\ y$ of (74), we separate (74) into real and imaginary parts as follows

$$\begin{aligned} 1 - a\int_0^\infty e^{-x\tau}cos(\theta_h + y\tau)q(\tau)d\tau = &- \varepsilon\ \delta_2\ a\int_0^\infty e^{-x\tau}cos(\theta_h + y\tau)q(\tau)d\tau \\ &- \frac{\varepsilon^2}{1+\varepsilon}\ \delta_2\ b\ d\ a\int_0^\infty e^{-x\tau}cos(\theta_\mu + \theta_h + y\tau)q(\tau)d\tau \\ &- \varepsilon\ \delta_1\int_0^\infty e^{-x\tau}cos(y\tau)p(\tau)d\tau, \end{aligned} \tag{75}$$

$$\begin{aligned} a\int_0^\infty e^{-x\tau}sin(\theta_h + y\tau)q(\tau)d\tau = &\varepsilon\ \delta_2\ a\int_0^\infty e^{-x\tau}sin(\theta_h + y\tau)q(\tau)d\tau \\ &+ \frac{\varepsilon^2}{1+\varepsilon}\ \delta_2\ b\ d\ a\int_0^\infty e^{-x\tau}sin(\theta_\mu + \theta_h + y\tau)q(\tau)d\tau \\ &+ \varepsilon\ \delta_1\int_0^\infty e^{-x\tau}sin(y\tau)p(\tau)d\tau. \end{aligned} \tag{76}$$

By the Rieman and Lebesgue Lemma, we find the facts similar to [3] below.

P1. If $x \geq 0, \mid y \mid + x \to \infty$, then

$$
\begin{aligned}
&\int_0^\infty e^{-x\tau} cos(y\tau)p(\tau)d\tau \to 0, \\
&\int_0^\infty e^{-x\tau} sin(y\tau)p(\tau)d\tau \to 0, \\
&\int_0^\infty e^{-x\tau} cos(y\tau)q(\tau)d\tau \to 0, \\
&\int_0^\infty e^{-x\tau} sin(y\tau)q(\tau)d\tau \to 0, \\
&\int_0^\infty e^{-x\tau} cos(\theta_h + y\tau)q(\tau)d\tau \to 0, \\
&\int_0^\infty e^{-x\tau} sin(\theta_h + y\tau)q(\tau)d\tau \to 0, \\
&\int_0^\infty e^{-x\tau} cos(\theta_\mu + \theta_h + y\tau)q(\tau)d\tau \to 0, \\
&\int_0^\infty e^{-x\tau} sin(\theta_\mu + \theta_h + y\tau)q(\tau)d\tau \to 0,
\end{aligned}
\tag{77}
$$

because $p(\tau), q(\tau)$ are of bounded variation.

P2. $\forall\, x \geq 0, y > 0$,

$$
\int_0^\infty e^{-x\tau} sin(y\tau)p(\tau)d\tau > 0, \tag{78}
$$

because $p(\tau)$ is nonincreasing.

As we show later, the follow results can be checked step by sep.

Result A.$(x, y) = (0, 0)$ is not the root of (75), (76).

Substituting $x = 0, y = 0$ into (75), it takes the form

$$
1 - \int_0^\infty q(\tau)d\tau = -\varepsilon\ \delta_2 \int_0^\infty q(\tau)a\tau - \frac{\varepsilon^2}{1+\varepsilon}\ \delta_2\ \frac{d}{\mu} \int_0^\infty q(\tau)d\tau - \varepsilon\ \delta_1 \int_0^\infty p(\tau)d\tau, \tag{79}
$$

i.e.,

$$
0 = -(\varepsilon + \frac{\varepsilon^2}{1+\varepsilon}\ \delta_2\ \frac{d}{\mu}), \tag{80}
$$

a contradiction appears in (80).So Result A is true.

Result B. (x,0) with $x > 0$ is not the root of (75) ,(76).

Substituting $y = 0$ into (75) , it takes the form

$$
\begin{aligned}
1 - a \int_0^\infty e^{-x\tau} q(\tau)d\tau = &- \varepsilon\ \delta_2\ a \int_0^\infty e^{-x\tau} q(\tau)d\tau \\
&- \frac{\varepsilon^2}{1+\varepsilon}\ \delta_2\ b\ d\ a \int_0^\infty e^{-x\tau} q(\tau)d\tau \\
&- \varepsilon\ \delta_2 \int_0^\infty e^{-x\tau} p(\tau)d\tau.
\end{aligned}
\tag{81}
$$

In this case,

$$
\begin{aligned}
&0 < a = \frac{h}{h+x} < 1, \\
&0 < b = \frac{1}{\mu+x} < \frac{1}{\mu}, \\
&0 < \int_0^\infty e^{-x\tau} q(\tau) d\tau < 1, \\
&0 < \int_0^\infty e^{-x\tau} p(\tau) d\tau < 1.
\end{aligned}
\tag{82}
$$

So the left-hand side of (81) is strictly positive,whereas the right-hand side of (81) is negative.This contradiction in (81) show that Result B is true.

Result C. There are no roots (x,y) of (75),(76) with $x \geq 0$ if ε is sufficiently close to 0.

Clearly, we only need to show roots (x,y) with $x \geq 0, y > 0$.

IF it does not hold,we have sequences ε_j, x_j, y_j satisfying (75), (76) with

$$\varepsilon_j > 0, \quad x_j \geq 0, \quad y_j > 0, \quad j = 1, 2, ...,$$

and

$$\varepsilon_j \to 0, \quad j \to \infty.$$

If $sup\{y_j\} = \infty$, then $\exists$ subsequence $y_{j'}$ of the sequence y_j with $y_{j'} \to \infty, j' \to \infty$. Substituting $x_{j'}, y_{j'}, \varepsilon_{j'}$ into (75) and let $j' \to \infty$,it takes the form $1 = 0$, a contradiction. So the sequence y_j is bounded,i.e.,

$$sup\{y_j\} < \infty. \tag{83}$$

Similarly,we find

$$sup\{x_j\} < \infty. \tag{84}$$

By (83),(84), $\exists$ subsequence $(x_{j''}, y_{j''})$ of the sequence (x_j, y_j) with

$$x_{j''} \to x_0, y_{j''} \to y_0, \varepsilon_{j''} \to 0, j'' \to \infty$$

and $x_0 \geq 0, y \geq 0$.

Case A. $x_0^2 + y_0^2 \neq 0$. Substituting $x_{j''}, y_{j''}, \varepsilon_{j''}$ into (75) and let $j'' \to \infty$, it takes the forms

$$1 - a(x_0, y_0) \int_0^\infty e^{-x_0\tau} cos(\theta_h(x_0, y_0) + y_0\tau) q(\tau) d\tau = 0,$$

i.e.,

$$1 = a(x_0, y_0) \int_0^\infty e^{-x_0\tau} cos(\theta_h(x_0, y_0) + y_0\tau) q(\tau) d\tau. \tag{85}$$

Paying attention to the follow inequalitys

$$\begin{aligned}
&| \int_0^\infty e^{-x_0\tau} cos(\theta_h(x_0, y_0) + y_0\tau) q(\tau) d\tau | \\
&\leq \int_0^\infty e^{-x_0\tau} q(\tau) d\tau \leq \int_0^\infty q(\tau) d\tau = 1, \\
&a(x_0, y_0) = \frac{h}{\sqrt{(h + x_0^2)^2 + y_0^2}} < 1,
\end{aligned}$$

we find a contradiction in (85) becauce of that the right-hand side of (85) is strictly lees than 1.

Case B. $x_0^2 + y_0^2 = 0$, i.e., $x_0 = 0, y_0 = 0$. Substituting $x_{j''}, y_{j''}, \varepsilon_{j''}$ into (76) and dividing by $y_{j''} > 0$, let $j'' \to \infty$, we find

$$\frac{1}{h} + \int_0^\infty \tau q(\tau) d\tau = 0, \tag{86}$$

a contradiction because of that the left-hand side of (86) is strictly positive.

So Result C is true.Further the proof end except the case $k(\tau) \equiv k(constant)$.

In fact,if $k(\tau) \equiv k(constant)$,the model (2) takes the form (1),the endemic equilibrium E^* is locally asymptotically stable(see [1]).

References

[1] Carlos Castillo-chavez and Zhilan Feng,To treat or not to treat:The case of tuberculosis, to publish;

[2] (to search)

[3] Horst R. Thieme and Carlos Castillo-chavez, How many infection-age-dependent infectivity affect the dynamics of HIV/AIDS? SIAM J.APPL.MATH.,Vol.53,No.5(1993). pp.1447 – 1479.